

FILE 'BIOSIS' ENTERED AT 11:05:05 ON 30 MAY 2004
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FILE 'MEDLINE' ENTERED AT 11:05:05 ON 30 MAY 2004

=> s petiard.in.

L1 1 PETIARD.IN.

=> d 11

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1988:587562 CAPLUS

DN 109:187562

TI The hypothesis of J. C. Mestre concerning variability in plant cell cultures: methods of approach

AU Vannereau, Agnes

CS Lab. Biol. Cell., Fac. Pharm., Chatenay-Malabry, 92296, Fr.

SO Lettres Botaniques (1988), (1), 41-8

CODEN: LEBODV; ISSN: 0181-1797

DT Journal; General Review

LA French

=> s 11 and cocoa

L2 0 L1 AND COCOA

=> s crouzillat.in.

L3 0 CROUZILLAT.IN.

=> s petiard.au.

L4 0 PETIARD.AU.

=> s crouzillat.au.

L5 0 CROUZILLAT.AU.

=> s gene###(10a) (cocoa or chocolate) (10a) (detect### or determin###)

L6 8 GENE###(10A) (COCOA OR CHOCOLATE) (10A) (DETECT### OR DETERMIN###)

=> s 16 and PCR

L7 4 L6 AND PCR

=> s 17 and (chitinase or mitochondrial### or choroplas###)

L8 2 L7 AND (CHITINASE OR MITOCHONDR### OR CHOROPLAS###)

=> d 18 1-2 bib ab kwic

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:609270 CAPLUS

DN 139:241115

TI Detection of hazelnut DNA traces in chocolate by PCR

AU Herman, Lieve; De Block, Jan; Viane, Ronald

CS Department for Animal Product Quality, Agricultural Research Centre, Melle, B-9090, Belg.

SO International Journal of Food Science and Technology (2003), 38(6), 633-640

CODEN: IJFTEZ; ISSN: 0950-5423

PB Blackwell Publishing Ltd.

DT Journal

LA English

AB By use of the Dneasy Plant Tissue kit (Qiagen Inc.) plant DNA could be extracted from chocolate and related matrixes. The polymerase chain reaction (PCR) detection of mitochondrial plant DNA is directly correlated with the length of the amplified fragment indicating shearing of DNA during chocolate production Hazelnut DNA could be specifically

detected in chocolate matrixes with primers derived from the intron between exon B and C of the **mitochondrial** gene nad1. Specificity was confirmed towards individual chocolate ingredients and in 20 hazelnut neg. chocolates. From taxonomically closely related plant species, only *Carpinus turczaninovii*, *Ostrya carpinifolia* and *Corylus americana* showed cross reaction, this was because of the identical sequence of the nad1 fragment. Application of extra MgCl₂ throughout the DNA extraction procedure and of a specially designed Mg²⁺ buffered PCR , increased the detection sensitivity of co-processed hazelnut in chocolate to 0.001% or 10 ppm.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Detection of hazelnut DNA traces in chocolate by PCR

AB By use of the Dneasy Plant Tissue kit (Qiagen Inc.) plant DNA could be extracted from chocolate and related matrixes. The polymerase chain reaction (PCR) detection of **mitochondrial** plant DNA is directly correlated with the length of the amplified fragment indicating shearing of DNA during chocolate production Hazelnut DNA could be specifically detected in chocolate matrixes with primers derived from the intron between exon B and C of the **mitochondrial** gene nad1. Specificity was confirmed towards individual chocolate ingredients and in 20 hazelnut neg. chocolates. From taxonomically closely related plant species, only *Carpinus turczaninovii*, *Ostrya carpinifolia* and *Corylus americana* showed cross reaction, this was because of the identical sequence of the nad1 fragment. Application of extra MgCl₂ throughout the DNA extraction procedure and of a specially designed Mg²⁺ buffered PCR , increased the detection sensitivity of co-processed hazelnut in chocolate to 0.001% or 10 ppm.

ST sequence plant **mitochondria** gene nad1 NADH dehydrogenase PCR; hazelnut contamination chocolate PCR food allergy

IT Food allergy
(PCR detection of hazelnut DNA traces in chocolate and potential use in minimizing contamination)

IT Chocolate
PCR (polymerase chain reaction)
(detection of hazelnut DNA traces in chocolate by PCR)

IT Genetic element
RL: ANT (Analyte); BUU (Biological use, unclassified); FFD (Food or feed use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(intron; PCR detection of hazelnut DNA traces in chocolate using primers derived from intron 2 of the **mitochondrial** gene nad1)

IT Gene, plant
RL: ANT (Analyte); BUU (Biological use, unclassified); FFD (Food or feed use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nad1; sequences of nad1 **mitochondrial** gene fragments from various plants, and uses thereof for PCR detection of hazelnut DNA in chocolate)

IT Beet (*Beta maritima*)
Corylus colurna
Ostrya carpinifolia
Soybean (*Glycine max*)
Theobroma cacao
(sequences of nad1 **mitochondrial** gene fragments from various plants, and uses thereof for PCR detection of hazelnut DNA in chocolate)

IT **Mitochondrial** DNA
RL: ANT (Analyte); BUU (Biological use, unclassified); FFD (Food or feed use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sequences of nad1 **mitochondrial** gene fragments from various plants, and uses thereof for PCR detection of hazelnut DNA in chocolate)

IT DNA sequences
Protein sequences

(sequences of nad1 mitochondrial gene fragments, and uses thereof for PCR detection of hazelnut DNA in chocolate)
 IT 487274-32-8, GenBank CAD21836 487274-33-9, GenBank CAD21838
 487274-34-0, GenBank CAD21837
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; sequences of nad1 mitochondrial gene fragments, and uses thereof for PCR detection of hazelnut DNA in chocolate)

IT 415263-96-6 415263-97-7 415263-98-8 415263-99-9 415264-00-5
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (nucleotide sequence; sequences of nad1 mitochondrial gene fragments, and uses thereof for PCR detection of hazelnut DNA in chocolate)

IT 9079-67-8, NADH dehydrogenase
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (subunit I; sequences of nad1 mitochondrial gene (NADH dehydrogenase) fragments from various plants, and uses thereof for PCR detection of hazelnut DNA in chocolate)

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:314432 CAPLUS
 DN 132:330582
 TI Use of DNA identification techniques for the determination of genetic material of cocoa in fermented or roasted beans and chocolate
 IN Petiard, Vincent; Crouzillat, Dominique
 PA Societe des Produits Nestle S.A., Switz.
 SO Eur. Pat. Appl., 20 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 999283	A1	20000510	EP 1998-121043	19981105
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 2000028078	A1	20000518	WO 1999-EP8268	19991029
	W: AU, BR, CA, CN, ID, IN, JP, MX, US, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9964759	A1	20000529	AU 1999-64759	19991029
	AU 762765	B2	20030703		
	BR 9915050	A	20010807	BR 1999-15050	19991029
	EP 1127158	A1	20010829	EP 1999-952637	19991029
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002529105	T2	20020910	JP 2000-581244	19991029
	ZA 2001004563	A	20020704	ZA 2001-4563	20010604
PRAI	EP 1998-121043	A	19981105		
	WO 1999-EP8268	W	19991029		
AB	The present invention presents mol. genetic techniques for detection of cocoa DNA in fermented and/or roasted cocoa beans, and in chocolate. The cocoa includes varieties that have been modified by common breeding techniques or modified by genetic engineering. Specifically, the invention presents the use of polymerase chain reaction (PCR), random amplified polymorphic DNA (RAPD), restriction fragment length polymorphism (RFLP) and microsatellite identification in detecting cocoa chloroplastic and/or mitochondrial DNA. The invention provides primers used in the amplification of the 5S rRNA intergenic spacer and seed storage protein (SSP) gene from cocoa. The sequences of SSP gene and 5S rRNA intergenic spacer-specific primers, as				

well as RAPD primers, were included in the invention.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present invention presents mol. **genetic** techniques for **detection** of **cocoa** DNA in fermented and/or roasted **cocoa** beans, and in chocolate. The **cocoa** includes varieties that have been modified by common breeding techniques or modified by genetic engineering. Specifically, the invention presents the use of polymerase chain reaction (PCR), random amplified polymorphic DNA (RAPD), restriction fragment length polymorphism (RFLP) and microsatellite identification in detecting **cocoa** chloroplastic and/or **mitochondrial** DNA. The invention provides primers used in the amplification of the 5S rRNA intergenic spacer and seed storage protein (SSP) gene from **cocoa**. The sequences of SSP gene and 5S rRNA intergenic spacer-specific primers, as well as RAPD primers, were included in the invention.

ST DNA chloroplast **mitochondria** detection **cocoa** fermented roasted bean chocolate; PCR RAPD RFLP **cocoa** DNA detection fermented roasted bean; chocolate **cocoa** DNA detection PCR RAPD RFLP; microsatellite **cocoa** DNA detection fermented roasted bean chocolate

IT Gene, plant
RL: ANT (Analyte); ANST (Analytical study)
(5S rRNA, intergenic spacer of; mol. **genetic** techniques (PCR, RAPD, RFLP and microsatellite identification) for **cocoa** DNA **detection** in fermented or roasted beans and chocolate)

IT Genetic element
RL: ANT (Analyte); ANST (Analytical study)
(IGS (intergenic spacer), of 5S RNA **gene**; mol. **genetic** techniques (PCR, RAPD, RFLP and microsatellite identification) for **cocoa** DNA **detection** in fermented or roasted beans and chocolate)

IT Cocoa products
(beans, roasted and/or fermented; mol. **genetic** techniques (PCR, RAPD, RFLP and microsatellite identification) for **cocoa** DNA **detection** in fermented or roasted beans and chocolate)

IT Confectionery
Confectionery
(dark **chocolate**; mol. **genetic** techniques (PCR, RAPD, RFLP and microsatellite identification) for **cocoa** DNA **detection** in fermented or roasted beans and chocolate)

IT Chocolate
Chocolate
(dark; mol. **genetic** techniques (PCR, RAPD, RFLP and microsatellite identification) for **cocoa** DNA **detection** in fermented or roasted beans and chocolate)

IT Gene, plant
RL: ANT (Analyte); ANST (Analytical study)
(for seed storage protein; mol. **genetic** techniques (PCR, RAPD, RFLP and microsatellite identification) for **cocoa** DNA **detection** in fermented or roasted beans and chocolate)

IT Microsatellite DNA
RL: ANT (Analyte); ANST (Analytical study)
(identification of; mol. **genetic** techniques (PCR, RAPD, RFLP and microsatellite identification) for **cocoa** DNA **detection** in fermented or roasted beans and chocolate)

IT Breeding, plant
Chloroplast
Cocoa (Theobroma cacao)
Genetic engineering
Mitochondria
PCR (polymerase chain reaction)

RAPD analysis
RFLP (restriction fragment length polymorphism)
(mol. genetic techniques (PCR, RAPD, RFLP and
microsatellite identification) for cocoa DNA
detection in fermented or roasted beans and chocolate)

IT DNA
RL: ANT (Analyte); ANST (Analytical study)
(mol. genetic techniques (PCR, RAPD, RFLP and
microsatellite identification) for cocoa DNA
detection in fermented or roasted beans and chocolate)

=> d 17 1-4

L7 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:609270 CAPLUS
DN 139:241115
TI Detection of hazelnut DNA traces in chocolate by PCR
AU Herman, Lieve; De Block, Jan; Viane, Ronald
CS Department for Animal Product Quality, Agricultural Research Centre,
Melle, B-9090, Belg.
SO International Journal of Food Science and Technology (2003), 38(6),
633-640
CODEN: IJFTEZ; ISSN: 0950-5423
PB Blackwell Publishing Ltd.
DT Journal
LA English
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:590944 CAPLUS
DN 139:145008
TI Genomic and cDNA sequences of mouse RAB38, RAB38 mutation detection, and
RAB38 function alteration to modulate mammalian pigmentation
IN Pavan, William J.; Loftus, Stacie K.
PA The Government of the Usa as Represented by the Secretary of the Dept.
of Health and Human Services, USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
	-----	-----	-----	-----	-----	
PI	WO 2003061580	A2	20030731	WO 2003-US1622	20030117	
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	PRAI US 2002-349929P	P	20020118			

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:813990 CAPLUS
DN 135:357065
TI Analysis procedure for the detection of cocoa husks in cocoa products.
IN Muench, Michael Anton; Schieberle, Peter; Fischer, Markus; Bacher,

Adelbert
PA Germany
SO Ger. Offen., 14 pp.
CODEN: GWXXBX

DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10019289	A1	20011108	DE 2000-10019289	20000419
PRAI	DE 2000-10019289		20000419		

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:314432 CAPLUS
DN 132:330582
TI Use of DNA identification techniques for the determination of genetic material of cocoa in fermented or roasted beans and chocolate
IN Petiard, Vincent; Crouzillat, Dominique
PA Societe des Produits Nestle S.A., Switz.
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW

DT Patent
LA English
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	WO 2000028078	A1	20000518	WO 1999-EP8268	19991029
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	BR 9915050	A	20010807	BR 1999-15050	19991029
	EP 1127158	A1	20010829	EP 1999-952637	19991029
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	JP 2002529105	T2	20020910	JP 2000-581244	19991029
	ZA 2001004563	A	20020704	ZA 2001-4563	20010604
PRAI	EP 1998-121043	A	19981105		
	WO 1999-EP8268	W	19991029		

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L6 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:609270 CAPLUS
DN 139:241115
TI Detection of hazelnut DNA traces in chocolate by PCR
AU Herman, Lieve; De Block, Jan; Viane, Ronald
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SO International Journal of Food Science and Technology (2003), 38(6),
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PB Blackwell Publishing Ltd.
DT Journal
LA English
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L6 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:590944 CAPLUS
 DN 139:145008
 TI Genomic and cDNA sequences of mouse RAB38, RAB38 mutation detection, and RAB38 function alteration to modulate mammalian pigmentation
 IN Pavan, William J.; Loftus, Stacie K.
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 SO PCT Int. Appl., 62 pp.
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 LA English
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2002-349929P	P	20020118		

L6 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
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 DN 135:357065
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 PA Germany
 SO Ger. Offen., 14 pp.
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 LA German
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PI	DE 10019289	A1	20011108	DE 2000-10019289	20000419
PRAI	DE 2000-10019289		20000419		

L6 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:470722 CAPLUS
 DN 133:72066
 TI Site specific molecular diagnosis using laser assisted microdissection technique
 AU Sato, Nakako; Aoyagi, Yasuyuki; Noguchi, Masayuki
 CS Grad. Sch. Med., Tsukuba Univ., Japan
 SO Byori to Rinsho (2000), 18(7), 624-627
 CODEN: BYRIEM; ISSN: 0287-3745
 PB Bunkodo
 DT Journal; General Review
 LA Japanese

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:314432 CAPLUS
 DN 132:330582
 TI Use of DNA identification techniques for the determination of genetic

material of cocoa in fermented or roasted beans and chocolate
 IN Petiard, Vincent; Crouzillat, Dominique
 PA Societe des Produits Nestle S.A., Switz.
 SO Eur. Pat. Appl., 20 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 999283	A1	20000510	EP 1998-121043	19981105
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 2000028078	A1	20000518	WO 1999-EP8268	19991029
	W: AU, BR, CA, CN, ID, IN, JP, MX, US, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9964759	A1	20000529	AU 1999-64759	19991029
	AU 762765	B2	20030703		
	BR 9915050	A	20010807	BR 1999-15050	19991029
	EP 1127158	A1	20010829	EP 1999-952637	19991029
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002529105	T2	20020910	JP 2000-581244	19991029
	ZA 2001004563	A	20020704	ZA 2001-4563	20010604
PRAI	EP 1998-121043	A	19981105		
	WO 1999-EP8268	W	19991029		
RE.CNT 5	THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD				
	ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1909:4262 CAPLUS
 DN 3:4262
 OREF 3:811c-e
 TI General Methods for the Detection of Adulteration in
 Cocoa and Chocolate
 AU Bordas; Touplain, F.
 CS Labs. of the Minister of Finance
 SO Annales des Falsifications et des Fraudes (1909), 1, 12-29
 CODEN: AFEFA4; ISSN: 0365-2157
 DT Journal
 LA Unavailable

L6 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2002:326471 BIOSIS
 DN PREV200200326471
 TI Analysis of vicilin (7S)-class globulin in cocoa cotyledons from various
 genetic origins.
 AU Amin, I.; Jinap, S. [Reprint author]; Jamilah, B.; Harikrisna, K.; Biehl,
 B.
 CS Faculty of Food Science and Biotechnology, Universiti Putra Malaysia, UPM
 Serdang, 43400, Selangor, Malaysia
 jinap@putra.upm.edu.my
 SO Journal of the Science of Food and Agriculture, (15 May, 2002) Vol. 82,
 No. 7, pp. 728-732. print.
 CODEN: JSFAAE. ISSN: 0022-5142.
 DT Article
 LA English
 ED Entered STN: 5 Jun 2002
 Last Updated on STN: 5 Jun 2002

L6 ANSWER 8 OF 8 MEDLINE on STN
 AN 79167434 MEDLINE
 DN PubMed ID: 436019

TI Inhibitory effect of cocoa powder on the growth of a variety of bacteria in different media.
AU Park C E; Stankiewicz Z K; Rayman M K; Hauschild A H
SO Canadian journal of microbiology, (1979 Feb) 25 (2) 233-5.
Journal code: 0372707. ISSN: 0008-4166.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197907
ED Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19790716

=> d 6-8 kwic
2 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):end

=> d 16 6-8 kwic

L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
TI General Methods for the Detection of Adulteration in
Cocoa and Chocolate

L6 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AB . . precursors of cocoa-specific aroma and are formed through
proteolysis during fermentation. High-resolution electrophoresis of
native proteins isolated from ripe, unfermented **cocoa** cotyledons
harvested from different cultivars was used to **determine**
genetic differences of the genotypes. Flavour differences have
been reported to exist after standard fermentation in cocoa beans
harvested from various. . .

L6 ANSWER 8 OF 8 MEDLINE on STN
AB The inhibitory effect of **cocoa** powder on 102 organisms belonging
to 13 **genera** was **determined**. All organisms tested
were inhibited by 5% cocoa. *Shigella*, *Staphylococcus*, *Micrococcus*, and
Bacillus were the most sensitive. The degree of. . .

=>

09/04/139

Freeform Search

US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
Database: EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Term: L11 and (PCR or RFLP)

Display: 10 Documents in Display Format: - Starting with Number 11

Generate: Hit List Hit Count Side by Side Image

Search History

DATE: Sunday, May 30, 2004 [Printable Copy](#) [Create Case](#)

<u>Set</u>	<u>Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
side by side				result set
		DB=USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
<u>L13</u>		L12 and (chitinase or mitochondr\$3 or choroplas\$3)	0	<u>L13</u>
<u>L12</u>		L11 and (PCR or RFLP)	20	<u>L12</u>
<u>L11</u>		(detect\$3 or determin\$3) same (gene\$3 or DNA or RNA or nucleic acid or oligonucleotide) same (cocoa or chocolate)	85	<u>L11</u>
<u>L10</u>		(detect\$3 or determin\$3) near5 (gene\$3 or DNA or ENA or nucleic acid or oligonucleotide\$1) near5 (cacao or chocolate)	0	<u>L10</u>
<u>L9</u>		gene\$3 near5 (cocoa or chocolate) near5 (detect3 or determin\$3)	2	<u>L9</u>
<u>L8</u>		L6 AND HYBRIDIZ\$5	0	<u>L8</u>
<u>L7</u>		L6 and PCR	1	<u>L7</u>
<u>L6</u>		L5 and cocoa	4	<u>L6</u>
<u>L5</u>		petiard.in.	36	<u>L5</u>
<u>L4</u>		L3 and PCR	1	<u>L4</u>
<u>L3</u>		L2 and cocoa	2	<u>L3</u>
<u>L2</u>		Crouzillat.in.	4	<u>L2</u>
<u>L1</u>		Petiard.pn.	0	<u>L1</u>

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PCR	42025
PCRS	1198
RAPD	413
RAPDS	431
RFLP	3595
RFLPS	1217
(8 AND (RAPD OR RFLP OR PCR)).USPT,EPAB,JPAB,DWPI.	8
(L8 AND (PCR OR RAPD OR RFLP)).USPT,EPAB,JPAB,DWPI.	8

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L9: Entry 4 of 8

File: USPT

Jul 23, 2002

DOCUMENT-IDENTIFIER: US 6423743 B1

TITLE: Cocoa extract compounds and methods for making and using the same

Drawing Description Text (28):

FIG. 15L shows the growth inhibition of Hela cells when treated with crude polyphenol extracts obtained from fermented cocoa beans and dried cocoa beans (stages throughout fermentation and sun drying; % control vs. concentration, .mu.g/mL; open circle is day zero fraction darkened circle is day 1 fraction, open inverted triangle is day 2 fraction, darkened inverted triangle is day 3 fraction, open square is day 4 fraction and darkened square is day 9 fraction);

Drawing Description Text (51):

FIG. 30A shows the substrate utilization during fermentation of cocoa beans;

Drawing Description Text (52):

FIG. 30B shows the metabolite production during fermentation;

Drawing Description Text (53):

FIG. 30C shows the plate counts during fermentation of cocoa beans;

Drawing Description Text (54):

FIG. 30D shows the relative concentrations of each component in fermented solutions of cocoa beans;

Detailed Description Text (6):

Additionally, Example 25 lists the heretofore never reported concentrations of the inventive compounds found in Theobroma and Herrania species and their inter- and intra-species crosses; and Example 25 also describes methods of modulating the amounts of the inventive compounds which may be obtained from cocoa by manipulating cocoa fermentation conditions.

Detailed Description Text (8):

The extracts, compounds and combinations of compounds derived therefrom having activity, without wishing to necessarily be bound by any particular theory, have been identified as cocoa polyphenol(s), such as procyanidins. These cocoa procyanidins have significant anti-cancer, anti-tumor or antineoplastic activity; antioxidant activity; inhibit DNA topoisomerase II enzyme and oxidative damage to DNA; possess antimicrobial activity; have the ability to modulate cyclo-oxygenase and/or lipoxygenase, NO or NO-synthase, apoptosis, platelet aggregation and blood or in vivo glucose, and have efficacy as non-steroidal antiinflammatory agents.

Detailed Description Text (51):

One significant property of COX-2 expressing cell lines is the enhanced expression of genes which participate in the modulation of apoptosis, i.e., programmed cell death. Several NSAIDs have been implicated in increased cell death and the induction of apoptosis in chicken embryo fibroblasts.

Detailed Description Text (70):

The role of NO in the immune system is different from its function in blood vessels. Macrophages contain a form of NOS that is inducible, rather than constitutive, referred to as iNOS. Transcription of the iNOS gene is controlled

both positively and negatively by a number of biological response modifiers called cytokines. The most important inducers are gamma-interferon, tumor necrosis factor, interleukin-1, interleukin-2 and lipopolysaccharide (LPS), which is a component of the cell walls of gram negative bacteria. Stimulated macrophages produce enough NO to inhibit ribonuclease reductase, the enzyme that converts ribonucleotides to the deoxyribonucleotides necessary for DNA synthesis. Inhibition of DNA synthesis may be an important way in which macrophages and other tissues possessing iNOS can inhibit the growth of rapidly dividing tumor cells or infectious bacteria.

Detailed Description Text (107):

Additionally, selective processing coupled with the identification of cocoa genotypes of interest could be used to prepare Standard-of-Identity (SOI) and non-SOI chocolate products as vehicles to deliver the active compounds to a patient in need of treatment for the disease conditions described above, as well as a means for the delivery of conserved levels of the inventive compounds.

Detailed Description Text (117):

Identification of Genes

Detailed Description Text (118):

A further embodiment of the invention comprehends the modulation of genes expressed as a result of intimate cellular contact by the inventive compounds or a combination of compounds. As such, the present invention comprehends methods for the identification of genes induced or repressed by the inventive compounds or a combination of compounds which are associated with several diseases, including but not limited to atherosclerosis, hypertension, cancer, cardiovascular disease, and inflammation. Specifically, genes which are differentially expressed in these disease states, relative to their expression in "normal" nondisease states are identified and described before and after contact by the inventive compounds or a combination of compounds.

Detailed Description Text (119):

As mentioned in the previous discussion, these diseases and disease states are based in part on free radical interactions with a diversity of biomolecules. A central theme in these diseases is that many of the free radical reactions involve reactive oxygen species, which in turn induce physiological conditions involved in disease progression. For instance, reactive oxygen species have been implicated in the regulation of transcription factors such as nuclear factor (NF)-.kappa.B. The target genes for NF-.kappa.B comprise a list of genes linked to coordinated inflammatory response. These include genes encoding tumor necrosis factor (TNF)-.alpha., interleukin (IL)-I, IL-6, IL-8, inducible NOS, Major Histocompatibility Complex (MHC) class I antigens, and others. Also, genes that modulate the activity of transcription factors may in turn be induced by oxidative stress. Oxidative stress is the imbalance between radical scavenging and radical generating systems. Several known examples (Winyard and Blake, 1997) of these conditions include gadd153 (a gene induced by growth arrest and DNA damage), the product of which has been shown to bind NF-IL6 and form a heterodimer that cannot bind to DNA. NF-IL6 upregulates the expression of several genes, including those encoding interleukins 6 and 8. Another example of oxidative stress inducible genes are gadd45 which regulates the effects of the transcription factor p53 in growth arrest. p53 codes for the p53 protein which can halt cell division and induce abnormal cells (e.g. cancer) to undergo apoptosis.

Detailed Description Text (120):

Given the full panoply of unexpected, nonobvious and novel utilities for the inventive compounds or combination of compounds for utility in a diverse array of diseases based in part by free radical mechanisms, the invention further comprehends strategies to determine the temporal effects on gene(s) or gene product(s) expression by the inventive compounds in animal in vitro and/or in vivo models of specific disease or disease states using gene expression assays. These assays

include, but are not limited to Differential Display, sequencing of cDNA libraries, Serial Analysis of Gene Expression (SAGE), expression monitoring by hybridization to high density oligonucleotide arrays and various reverse transcriptase-polymerization chain reaction (RT-PCR) based protocols or their combinations (Lockhart et al., 1996).

Detailed Description Text (121):

The comprehensive physiological effects of the inventive compounds or combination of compounds embodied in the invention, coupled to a genetic evaluation process permits the discovery of genes and gene products, whether known or novel, induced or repressed. For instance, the invention comprehends the *in vitro* and *in vivo* induction and/or repression of cytokines (e.g. IL-1, IL-2, IL-6, IL-8, IL-12, and TNF-.alpha.) in lymphocytes using RT-PCR. Similarly, the invention comprehends the application of Differential Display to ascertain the induction and/or repression of select genes; for the cardiovascular area (e.g. superoxide dismutase, heme oxidase, COX I and 2, and other oxidant defense genes) under stimulated and/or oxidant stimulated conditions (e.g. TNF-.alpha. or H₂O₂) conditions. For the cancer area, the invention comprehends the application of Differential Display to ascertain the induction and/or repression of genes or gene products such as CuZn-superoxide dismutase, Mn-superoxide dismutase, catalase, etc., in control and oxidant stressed cells.

Detailed Description Text (214):

Another series of assays were performed on crude polyphenol extracts prepared on a daily basis from a one ton scale traditional 5-day fermentation of Brazilian cocoa beans, followed by a 4-day sun drying stage. The results shown in FIG. 15L showed no obvious effect of these early processing stages, suggesting little change in the composition of the polyphenols. However, it is known (Lehrian and Patterson, 1983) that polyphenol oxidase (PPO) will oxidize polyphenols during the fermentation stage. To determine what effect enzymatically oxidized polyphenols would have on activity, another experiment was performed. Crude PPO was prepared by extracting finely ground, unfermented, freeze dried, defatted Brazilian cocoa beans with acetone at a ratio of 1 gm powder to 10 mL acetone. The slurry was centrifuged at 3,000 rpm for 15 min. This was repeated three times, discarding the supernatant each time with the fourth extraction being poured through a Buchner filtering funnel. The acetone powder was allowed to air dry, followed by assay according to the procedures described by McLord and Kilara, (1983). To a solution of crude polyphenols (100 mg/10 mL Citrate-Phosphate buffer, 0.02M, pH 5.5) 100 mg of acetone powder (4,000 units activity/mg protein) was added and allowed to stir for 30 min. with a stream of air bubbled through the slurry. The sample was centrifuged at 5,000 times g for 15 min. and the supernatant extracted 3 times with 20 mL ethyl acetate. The ethyl acetate extracts were combined, taken to dryness by distillation under partial vacuum and 5 mL water added, followed by lyophilization. The material was then assayed against HeLa cells and the dose-response compared to crude polyphenol extracts that were not enzymatically treated. The results (FIG. 15M) showed a significant shift in the dose-response curve for the enzymatically oxidized extract, showing that the oxidized products were more inhibitory than their native forms.

Detailed Description Text (218):

To determine whether cocoa extracts containing procyanidins possessed antioxidant properties, a standard Rancimat method was employed. The procedures described in Examples 1, 2 and 3 were used to prepare cocoa extracts which were manipulated further to produce two fractions from gel permeation chromatography. These two fractions are actually combined fractions A through C, and D and E (See FIG. 1) whose antioxidant properties were compared against the synthetic antioxidants BHA and BHT.

Detailed Description Text (341):

Obtaining Desired Procyanidins Via Manipulating Fermentation

Detailed Description Text (342) :

Microbial strains representative of the succession associated with cocoa fermentation were selected from the M&M/Mars cocoa culture collection. The following isolates were used: Acetobacter aceti ATCC 15973 Lactobacillus sp. (BH 42) Candida cruzii (BA 15) Saccharomyces cerevisiae (BA 13) Bacillus cereus (BE 35) Bacillus sphaericus (ME 12)

Detailed Description Text (345) :

The bench scale fermentation was performed in duplicate. All treatments were incubated as indicated below: Day 1: 26.degree. C. Day 2: 26.degree. C. to 50.degree. C. Day 3: 50.degree. C. Day 4: 45.degree. C. Day 5: 40.degree. C.

Detailed Description Text (346) :

The model fermentation was monitored over the duration of the study by plate counts to assess the microbial population and HPLC analysis of the fermentation medium for the production of microbial metabolites. After treatment, the beans were dried under a laminar flow hood to a water activity of 0.64 and were roasted at 66.degree. C. for 15 min. Samples were prepared for procyanidin analysis. Three beans per treatment were ground and defatted with hexane, followed by extraction with an acetone:water:acetic acid (70:29.5:0.5%) solution. The acetone solution extract was filtered into vials and polyphenol levels were quantified by normal phase HPLC as in Example 13, method B. The remaining beans were ground and tasted. The cultural and analytical profiles of the model bench-top fermentation process is shown in FIGS. 30A-C. The procyanidin profiles of cocoa beans subjected to various fermentation treatments is shown in FIG. 30D.

Detailed Description Text (347) :

This Example demonstrates that the invention need not be limited to any particular cocoa genotype; and, that by manipulating fermentation, the levels of procyanidins produced by a particular Theobroma or Herrania species or their inter or intra species specific crosses thereof can be modulated, e.g., enhanced.

Detailed Description Text (360) :

Using blood glucose levels as an indicator for the signal events which occur in vivo for the regulation of appetite and satiety, a series of simple experiments were conducted using a healthy male adult volunteer age 48 to determine whether cocoa polyphenols would modulate glucose levels. Cocoa polyphenols were partially purified from Brazilian cocoa beans according to the methods described by Clapperton et al. (1992). This material contained no caffeine or theobromine. Fasting blood glucose levels were analyzed on a timed basis after ingestion of 10 fl. oz of Dexicola 75 (caffeine free) Glucose tolerance test beverage (Curtin Matheson 091-421) with and without 75 mg cocoa polyphenols. This level of polyphenols represented 0.1% of the total glucose of the test beverage and reflected the approximate amount that would be present in a standard 100 g chocolate bar. Blood glucose levels were determined by using the Accu-Chek III blood glucose monitoring system (Boehringer Mannheim Corporation). Blood glucose levels were measured before ingestion of test beverage, and after ingestion of the test beverage at the following timed intervals: 15, 30, 45, 60, 75, 90, 120 and 180 minutes. Before the start of each glucose tolerance test, high and low glucose level controls were determined. Each glucose tolerance test was performed in duplicate. A control test solution containing 75 mg cocoa polyphenols dissolved in 10 fl. oz. distilled water (no glucose) was also performed.

Detailed Description Text (403) :

FIG. 55 indicates that only procyanidin fraction C, at 100 .mu.g/mL, could induce NO production by monocytes/macrophages. Basal NO production by these cells was undetectable and no nitrite could be detected in any of the cocoa procyanidin fractions used at 100 .mu.g/mL. FIG. 56 indicates that procyanidin fractions A and D enhanced LPS-induced NO production by .UPSILON.-interferon primed

monocytes/macrophages. Procyanidin fraction C was marginally effective, since LPS-stimulated monocytes/macrophages cultured in the absence of procyanidin fractions produced only 4 .mu.mole/10⁵ cells/48 hours. .UPSILON.-Interferon alone was ineffective in inducing NO.

Detailed Description Text (478):

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82. Gali, H. U., Perchellet, E. M., Klish, D. S., Johnson, J. M. and Perchellet, J-P. Antitumor-promoting activities of hydrolyzable tannins in mouse skin, *Carcinogenesis*, 13: 4, 715-718 (1992). 83. Tabib, K., Besancon, P. and Rouanet, J-M. Dietary Grape seed Tannins Affect Lipoproteins, Lipoprotein Lipases and Tissue Lipids in Rats Fed Hypercholesterolemic Diet's, *J. Nutrition*, 124:12, 2451-2457. 84. Paolino, V. J. and Kashket, S. Inhibition by Cocoa Extracts of Biosynthesis of Extracellular Polysaccharide by Human Oral Bacteria, *Archs. Oral Biol.* 30:4, 359-363 (1985). 85. Lockhart, D. J., Dong, H., Byrne, M. C., Follettie, M. T., Gallo, M. V., Chee, M. S., Mittmann, M., Wang, C., Kobayashi, M., Horton, H., and Brown, E. L., Expression monitoring by hybridization to high-density oligonucleotide arrays, *Nature Biotech.*, 14, 1675-1680 (1996). 86. Kreiner, T. Rapid genetic sequence analysis using a DNA probe array system, *Am. Lab.*, March, 1996. 87. Lipshutz, R. J., Morris, D., Chee, M., Hubbell, E., Kozal, M. J., Shah, N., Shen, N., Yang, R. and Fodor, S. P. A. Using oligonucleotide Probe Arrays to Access Genetic Diversity, *Biotechniques*, 19: 3, 442-447 (1995). 88. Borman, S. DNA Chips Come of Age, *Chem. & Eng. News*, 42-43, Dec. 9, 1996 89. Tahara, H., Mihara, Y., Ishii, Y., Fujiwara, M., Endo, H., Maeda, S and Ide, T. Telomerase Activity in Cellular Immortalization, *Cell Structure and Function*, 20: 6, 1B-1615 (1995). 90. Heller, K., Kilian, A., Paityszek, M. A., and Kleinhofs, A. Telomerase activity in plant extracts, *Mol. Gen. Genet.* 252, 342-345 (1996). 91. Goffeau, A. Molecular fish fish on chips, *Nature*, 385, 202-203 (1997). 92. Friedrich, G. A. Moving beyond the genome projects, *Nature Biotechnology*, 14, 1234-1237 (1996). 93. Blanchard, R. K. and Cousins, R. J. Differential display of intestingal mRNAs regulated by dietary zinc., *Proc. Natl. Acad. Sci. USA*, 93, 6863-6868 (1996). 94. Pennisi, E. opening the Way to Gene Activity, *Science*, 275: 155-157 (1997). 95. Medlin, J. The Amazing Shrinking Laboratory, *Environmental Healt Perspectives*, 103: 3, 244-246. 96. Luehrsen, K. R., Marr, L. L., van der Knaap, E. and Cumberledge, S. Analysis of Differential Display RT-PCR Products Using Fluorescent Primers and GENESCAN Software, *Biotechniques*, 22: 1, 168-174. 97. Geiss, F., Heinrich, M., Hunkler, D. and Rimpler, H. Proanthocyanidins with (+)-Epicatechin Units from *Byronima Crassifolia* Bark, *Phytochemistry*, 39: 1, 635-643 (1995). 98. Iibuchi, S., Minoda, Y. and Yamada, K. Studies on Tannin Acyl Hydrolase of Microorganisms, Part II. A New Method Determining the Enzyme Activity Using the Change of Ultra Violet Absorption, *Agr. Biol. Chem.* 31: 5, 513-518 (1967). 99. Ferreira, D., Steynberg, J. P., Roux, D. G. and Brandt, E. V. Diversity of Structure and Function in Oligomeric Flavanoids, *Tetrahedron*, 48: 10, 1743-1803 (1992).

Detailed Description Paragraph Table (23) :

Fermentation Model Water Ethanol/acid infusate Fermentation daily daily transfer to daily transfer bench scale transfer solutions of to fermented model to fresh alcohol and acid pulp fermentation in water corresponding to pasteurized on sterile pulp levels determined each successive coinoculated at each stage of day of with test a model pulp fermentation strains fermentation

Detailed Description Paragraph Table (27) :

Monomers	Dimers	Trimers	Tetramers	Pentamers	Hexamers	Higher	Total	Unfermented	13,440
13,440	6,425	6,401	5,292	4,236	3,203	5,913	44,910	<u>Fermented</u>	2,695
470	301	277	7,383	<u>Roasted</u>	2,656	1,597	921	337	164
1,446	881	442	184	108	ND	5,866	Cocoa Hulls	114	53
1%	Fat	506	287	112	ND	ND	ND	915	Cocoa Powder
3,473	Red Dutch Cocoa	1,222	483	103	ND	ND	ND	1,808	Powder, pH 7.4, 11% fat Red
Dutch Cocoa	168	144	60	ND	ND	ND	372	Powder, pH 8.2, 23% fat	ND* = None detected.

Other Reference Publication (34):

Porter, L.J., Ma, Z. and Chan, B.G., "Cocoa Procyanoindins: Major Flavanoids and Identification of Some Minor Metabolites," *Phytochemistry*, 30, 1657-1663 (1991).

CLAIMS:

1. An assay for identifying at least one gene induced or repressed by a procyanoindin monomer and/or oligomer comprising a gene expression assay and a procyanoindin monomer monomer and/or oligomer obtained from a natural source.
9. An assay for identifying at least one gene induced or repressed by a procyanoindin monomer and/or oligomer comprising a gene expression assay and a synthetically prepared procyanoindin monomer and/or oligomer.
14. The assay of claim 1, wherein the induction or repression of the gene is associated with at least one of the following diseases: atherosclerosis, hypertension, cancer, cardiovascular disease, inflammation.
15. The assay of claim 9, wherein the induction or repression of the gene is associated with at least one of the following diseases: atherosclerosis, hypertension, cancer, cardiovascular disease, inflammation.
16. An assay for identifying at least one gene induced or repressed by a polymeric compound of the formula A.sub.n comprising a gene expression assay and the polymeric compound of the formula A.sub.n wherein A is a monomer of the following formula: ##STR9##

wherein n is an integer from 2-18, such that there is at least one terminal monomeric unit A, and one or a plurality of additional monomeric units R is 3-(.alpha.)-OH, 3-(.beta.)-OH, 3-(.alpha.)-O-sugar, or 3-(.beta.)-O-sugar; bonding between adjacent monomers takes place at positions selected from the group consisting of 4, 6, and 8; a bond for additional monomeric unit in position 4 has alpha or beta stereochemistry; X, Y, and Z are selected from the group consisting of monomeric unit A, hydrogen, and a sugar, with the provisos that as to at least one terminal monomeric unit, bonding of the additional monomeric unit thereto is at position 4 and optionally Y=Z=hydrogen; the sugar is optionally substituted with a phenolic moiety, and

pharmaceutically acceptable salts, derivatives thereof, oxidation products thereof, or combinations thereof.

17. The assay of claim 16 wherein said gene expression assay is selected from the group consisting of Differential Display assay, Serial Analysis of Gene Expression assay and expression monitoring by hybridization to high density oligonucleotide arrays.
18. The assay of claim 16, wherein the induction or repression of the gene is associated with at least one of the following diseases: atherosclerosis, hypertension, cancer, cardiovascular disease, inflammation.

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(FILE 'HOME' ENTERED AT 11:04:44 ON 30 MAY 2004)

FILE 'CAPLUS, BIOSIS, MEDLINE' ENTERED AT 11:05:05 ON 30 MAY 2004

L1 1 S PETIARD.IN.
L2 0 S L1 AND COCOA
L3 0 S CROUZILLAT.IN.
L4 0 S PETIARD.AU.
L5 0 S CROUZILLAT.AU.
L6 8 S GENE### (10A) (COCOA OR CHOCOLATE) (10A) (DETECT### OR DETERMIN##
L7 4 S L6 AND PCR
L8 2 S L7 AND (CHITINASE OR MITOCHONDR### OR CHOROPLAS###)
L9 13736 S (DETECT### OR DETERMIN###) (10A) (CHITINATSE OR MITOCHONDR### O
L10 1 S L9 AND COCOA
L11 434 S (DETECT### OR DETERMIN### OR DECID###) (10A) COCOA
L12 28 S L11 AND GENE###
L13 5 S L12 AND (PCR OR RFLP)
L14 1 S L13 AND (CHITINASE OR MITOCHONDR### OR CHLOROPLAS### OR SEED
L15 246 S (DETEC### OR DETERMIN### OR DECID###) (10A) COCOA
L16 16 S L15 AND GENE###
L17 12 DUP REM L16 (4 DUPLICATES REMOVED)